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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/058,024	01/29/2002	Anjana Rao	01997.001700.	2671

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EXAMINER	
BYRD, DEVON R	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/058,024	RAO ET AL.	
	Examiner	Art Unit	FILE COPY
	Devon R Byrd	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2002* .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-45* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

STATUS OF THE CLAIMS

CLAIMS 1-45 ARE PENDING IN THE PRESENT APPLICATION AND ARE SUBJECT TO RESTRICTION/ELECTION OF SPECIES REQUIREMENTS.

ELECTION/RESTRICTIONS

RESTRICTION TO ONE OF THE FOLLOWING INVENTIONS IS REQUIRED UNDER 35 U.S.C. 121:

I. CLAIMS 1-11, DRAWN TO A METHOD OF SCREENING FOR TEST COMPOUNDS CAPABLE OF MODULATING THE ACTIVITY OF AN ANERGY MARKER PROTEIN, CLASSIFIED IN CLASS 436, SUBCLASS 501.

II. CLAIMS 12-22, DRAWN TO A METHOD OF SCREENING FOR TEST COMPOUNDS CAPABLE OF MODULATING THE EXPRESSION LEVEL OF AN ANERGY MARKER, CLASSIFIED IN CLASS 435, SUBCLASS 6 TO THE EXTENT THAT THE METHOD IS DIRECTED TO NUCLEIC ACIDS.

III. CLAIMS 12-22, DRAWN TO A METHOD OF SCREENING FOR TEST COMPOUNDS CAPABLE OF MODULATING THE EXPRESSION LEVEL OF AN ANERGY MARKER, CLASSIFIED IN CLASS 435, SUBCLASS 6 TO THE EXTENT THAT THE METHOD IS DIRECTED TO PROTEINS.

IV. CLAIMS 23-38, DRAWN TO A METHOD OF SCREENING FOR TEST COMPOUNDS CAPABLE OF INHIBITING AN IMMUNE DISORDER, CLASSIFIED IN CLASS 435, SUBCLASS 70.1, TO THE EXTENT THAT THE METHOD IS DIRECTED TO NUCLEIC ACIDS.

V. CLAIMS 23-38, DRAWN TO A METHOD OF SCREENING FOR TEST COMPOUNDS CAPABLE OF INHIBITING AN IMMUNE DISORDER, CLASSIFIED IN CLASS 435, SUBCLASS 70.1, TO THE EXTENT THAT THE METHOD IS DIRECTED TO PROTEINS.

VI. CLAIMS 39-45, DRAWN TO A METHOD OF SCREENING TEST COMPOUNDS FOR INHIBITORS OF AN IMMUNE DISORDER IN A SUBJECT, CLASSIFIED IN CLASS 514, SUBCLASS 885 TO THE EXTENT THAT THE METHOD IS DIRECTED TO NUCLEIC ACIDS.

VII. CLAIMS 39-45, DRAWN TO A METHOD OF SCREENING TEST COMPOUNDS FOR INHIBITORS OF AN IMMUNE DISORDER IN A SUBJECT, CLASSIFIED IN CLASS 514, SUBCLASS 885 TO THE EXTENT THAT THE METHOD IS DIRECTED TO PROTEINS.

RESTRICTION IS DEEMED PROPER BECAUSE THE ABOVE METHODS CONSTITUTE PATENTABLY DISTINCT INVENTIONS FOR THE FOLLOWING REASONS: GROUPS I-VII ARE DIRECTED TO METHODS THAT RECITE STRUCTURALLY AND FUNCTIONALLY DISTINCT ELEMENTS, ARE NOT REQUIRED FOR ONE ANOTHER, AND ACHIEVE DIFFERENT GOALS.

GROUPS I, III, V AND VII ARE DRAWN TO THE USE OF ANERGY MARKER PROTEINS WHICH VARY IN LENGTH AND AMINO ACID CONTENT AND THUS CONSTITUTE PATENTABLY DISTINCT COMPOUNDS WHICH MAY POSSESS DIFFERENT PHYSICOCHEMICAL PROPERTIES AND/OR METHODS OF MANUFACTURE.

GROUPS II, IV, AND VI ARE DRAWN TO THE USE OF ANERGY MARKER POLYNUCLEOTIDES THAT VARY IN LENGTH AND NUCLEIC ACID CONTENT AND THUS CONSTITUTE PATENTABLY DISTINCT COMPOUNDS WHICH MAY POSSESS DIFFERENT PHYSICOCHEMICAL PROPERTIES AND/OR METHODS OF MANUFACTURE.

ADDITIONALLY, THE USE OF "NATURALLY-OCCURRING COMPOUNDS, BIOMOLECULES, PROTEINS, PEPTIDES, OLIGOPEPTIDES, POLYSACCHARIDES, NUCLEOTIDES AND POLYNUCLEOTIDES" IN METHODS OF THE CLAIMED INVENTION DOES NOT CONSTITUTE THE USE OF COMPOUNDS WHICH CONTAIN A COMMON CORE STRUCTURE ESSENTIAL TO A COMMON UTILITY (E.G., IMPROPER

Markush groups). Further, the use of functional language (e.g., "capable of modulating", "capable of inhibiting") to encompass compounds which differ markedly in structure (e.g., "biomolecules", proteins, polysaccharides, polynucleotides) represent improper Markush groupings which additionally lack a core which elicits a single common utility.

Likewise, the use of "an antigen, an antigen presenting cell, an activator of NFAT-NFAT ligand signaling, a combination of anti-CD3 and anti-CD28 antibodies, and a combination of anti-TCR and anti-CD28 antibodies" in methods of the claimed invention does not constitute the use of compounds which contain a common core structure essential to a common utility (e.g., improper Markush groups).

Further Restriction (This is not a species election)

Upon selection of any of Groups I-VII, Applicant must elect a specific subgeneric class of test compound (i.e., as disclosed on p 7 of the specification, (e.g., a nucleic acid (e.g., an antisense nucleic acid or ribozyme), a polypeptide (e.g., an antibody or an antigen-binding fragment thereof), a peptide fragment, a peptidomimetic, or a small molecule (e.g., a small organic molecule with molecular weight less than about 2000 or 800 Daltons)). With respect to variants which may encompass patentably distinct compounds within the elected subgeneric class of test compound, Applicant must elect a single variant that embodies a core structure directed to a common utility.

Group I

Upon selection of Group I, Applicant must then elect ***A SINGLE*** specific "anergy marker" from among those listed in Applicant's "Group I and Group II and Group III

AND GROUP IV", INCLUSIVE, EXPLICITLY DESIGNATE THAT ELECTION BY SEQ ID NO., **AND** DESIGNATE THE SPECIFIC PRIMARY STRUCTURE AND/OR AMINO ACID SEQUENCE OF THE "ANERGY MARKER PROTEIN" ENCODED BY THE ELECTED "ANERGY MARKER". APPLICANT MUST FURTHER ELECT A SINGLE SPECIFIC ACTIVITY OF SAID ELECTED ANERGY MARKER PROTEIN THAT IS CAPABLE OF BEING MODULATED BY SAID ELECTED TEST COMPOUND, WHEREIN BINDING INDICATES THAT THE TEST COMPOUND IS CAPABLE OF MODULATING THE ACTIVITY OF THE ANERGY MARKER PROTEIN.

FURTHER, UPON SELECTION OF GROUP I, APPLICANT MUST ELECT A METHOD TO DETECT BINDING ACTIVITY BETWEEN THE ELECTED TEST COMPOUND AND "ANERGY MARKER PROTEIN" (E.G., FLUORESCENCE-BASED TECHNOLOGY SUCH AS BRET, FRET, CYTOSENSOR MICROPHYSIOMETRY, FLIPR, LABEL-FREE PLASMON RESONANCE TECHNOLOGY), **AND** THE APPROPRIATE DIAGNOSTIC ANALYSIS TO BE PERFORMED TO ELUCIDATE THE COUPLING SYSTEMS (SEE P 124-125 OF THE SPECIFICATION).

GROUPS II AND III

UPON SELECTION OF GROUP II OR III, APPLICANT MUST THEN ELECT ***A SINGLE*** SPECIFIC "ANERGY MARKER" FROM AMONG THOSE LISTED IN APPLICANT'S "GROUP I AND GROUP II AND GROUP III AND GROUP IV", INCLUSIVE, AND EXPLICITLY DESIGNATE THAT ELECTION BY SEQ ID NO., **AND** DESIGNATE THE SPECIFIC PRIMARY STRUCTURE AND/OR AMINO ACID SEQUENCE OF THE "ANERGY MARKER PROTEIN" ENCODED BY THE ELECTED "ANERGY MARKER".

APPLICANT MUST FURTHER ELECT A SINGLE SPECIFIC "SAMPLE OF CELLS", WHEREIN A SUBSTANTIALLY MODULATED LEVEL OF EXPRESSION OF THE ANERGY MARKER IS AN INDICATION THAT THE TEST COMPOUND IS CAPABLE OF MODULATING THE LEVEL OF EXPRESSION (E.G., T CELLS OR B CELLS) SEE SPECIFICATION, P 18). UPON SUCH ELECTION, APPLICANT MUST FURTHER ELECT A SINGLE SPECIFIC SUBTYPE OF CELLS (E.G., T CELLS, E.G., TH1 CELLS, T CELLS WITH A

PARTICULAR T CELL RECEPTOR, T CELLS OF VARIOUS STAGES OF MATURATION, HELPER T CELLS, KILLER T CELLS; E.G., AS DISCLOSED ON P 18 OF THE SPECIFICATION).

FURTHER, UPON SELECTION OF GROUP II OR III, APPLICANT MUST ELECT A METHOD OF COMPARING ANERGY MARKER EXPRESSION LEVELS (E.G., DETECTION OF THE PRESENCE OF AN RNA SPECIES TRANSCRIBED FROM A SPECIFIC GENE, SPLICING OF THE RNA, E.G., BY NORTHERN BLOT ANALYSIS, RT-PCR OR GENECHIP; SEE P 152 OF THE SPECIFICATION). APPLICANT MUST THEN ELECT A SPECIFIC QUANTITATIVE RANGE DELINEATING "A FIRST LEVEL OF EXPRESSION" AND "A SECOND LEVEL OF EXPRESSION" OF AN ANERGY MARKER THAT IS CONSONANT WITH THE CLAIMED METHOD OF GROUP II OR III.

UPON SELECTION OF GROUP II OR III, APPLICANT MUST ELECT A SPECIFIC SUBGENERIC CLASS OF STIMULANT (I.E., AS DISCLOSED ON P 27 OF THE SPECIFICATION; E.G., AN ANTIGEN, AN ANTIGEN PRESENTING CELL, AN ACTIVATOR OF NFAT-NFAT LIGAND SIGNALING, A COMBINATION OF ANTI-CD3 AND ANTI-CD28 ANTIBODIES, AND/OR A COMBINATION OF ANTI-TCR AND ANTI-CD28 ANTIBODIES, IONOMYCIN AND/OR PMA). WITH RESPECT TO VARIANTS WHICH MAY ENCOMPASS PATENTABLY DISTINCT COMPOUNDS WITHIN THE ELECTED SUBGENERIC CLASS OF TEST COMPOUND, APPLICANT MUST ELECT A SINGLE VARIANT THAT EMBODIES A CORE STRUCTURE DIRECTED TO A COMMON UTILITY.

<u>GROUPS IV AND V</u>

UPON SELECTION OF GROUP IV OR V, APPLICANT MUST ELECT A SINGLE SPECIFIC IMMUNE DISORDER (E.G., AS DISCLOSED ON P 72 OF THE SPECIFICATION). IN ADDITION, APPLICANT MUST ELECT A SINGLE SPECIFIC PANEL OF ANERGY MARKERS COMPRISING A SINGLE SPECIFIC ANERGY MARKER (AND HOMOLOGS THEREOF; SEE P 66, LNS 10-12 OF THE SPECIFICATION) AS SET FORTH IN APPLICANT'S "GROUP I AND GROUP II AND GROUP III AND GROUP IV", INCLUSIVE, AND EXPLICITLY DESIGNATE THAT ELECTION BY SEQ ID NO. TO THE EXTENT THAT THE CLAIMED METHOD

is directed to proteins, Applicant must designate the specific primary structure and/or amino acid sequence of anergy marker proteins encoded by the elected anergy marker panel.

Further, upon selection of Group IV or V, Applicant must elect a method to detect binding activity between the elected test compound and the elected panel of anergy marker proteins (e.g., fluorescence-based technology such as BRET, FRET, cytosensor microphysiometry, FLIPR, label-free plasmon resonance technology), **AND** the appropriate diagnostic analysis to be performed to elucidate the coupling systems (see p 124-125 of the specification). In addition, Applicant must then elect a specific quantitative range delineating an "amount of binding" of the elected test compound to the elected anergy marker panel, wherein said "amount of binding" indicates that said elected test compound is capable of inhibiting said elected immune disorder.

Groups VI and VII

Upon selection of Group VI or VII, Applicant must elect a single specific immune disorder (e.g., as disclosed on p 72 of the specification), a single specific sample comprising cells, and a single specific cell type encompassed by said elected sample. Applicant must then elect ***A SINGLE*** specific "anergy marker" from among those listed in Applicant's "Group I and Group II and Group III and Group IV", inclusive, and explicitly designate that election by SEQ ID No., **AND** designate the specific primary structure and/or amino acid sequence of the "anergy marker protein" encoded by the elected "anergy marker".

Because these inventions are distinct for the reasons given above, and

A. HAVE ACQUIRED A SEPARATE STATUS IN THE ART AS SHOWN BY THEIR DIFFERENT CLASSIFICATION;

B. HAVE DIFFERENT AND SEPARATELY BURDENSOME MANUAL AND/OR COMPUTER STRUCTURE, NAME, AND BIBLIOGRAPHICAL SEARCHES; AND,

C. HAVE DIVERGENT SUBJECT MATTER; AND

D. SINCE THE LACK OF CHEMICAL COMPOUND STRUCTURE AND/OR A COMMON CORE RENDERS THE SEARCH UNDULY BURDENSOME (FOR EXAMPLE, SEARCHING PURELY FUNCTIONAL CLAIMS, (E.G., "CAPABLE OF MODULATING THE ACTIVITY OF" OR "CAPABLE OF INHIBITING") OR CLAIMS THAT READ ON MULTIPLE TYPES OF CHEMICAL COMPOUNDS (E.G., NUCLEIC ACIDS, PROTEINS, SMALL MOLECULES, ETC.) IS FUTILE);

RESTRICTION FOR EXAMINATION PURPOSES AS INDICATED IS PROPER.

APPLICANT IS ADVISED THAT THE REPLY TO THIS REQUIREMENT TO BE COMPLETE MUST INCLUDE AN ELECTION OF THE INVENTION TO BE EXAMINED EVEN THOUGH THE REQUIREMENT BE TRAVERSED (37 CFR 1.143).

APPLICANT IS REMINDED THAT UPON THE CANCELLATION OF CLAIMS TO A NON-ELECTED INVENTION, THE INVENTORSHIP MUST BE AMENDED IN COMPLIANCE WITH 37 CFR 1.48(B) IF ONE OR MORE OF THE CURRENTLY NAMED INVENTORS IS NO LONGER AN INVENTOR OF AT LEAST ONE CLAIM REMAINING IN THE APPLICATION. ANY AMENDMENT OF INVENTORSHIP MUST BE ACCOMPANIED BY A REQUEST UNDER 37 CFR 1.48(B) AND BY THE FEE REQUIRED UNDER 37 CFR 1.17(I).

ELECTION OF SPECIES

THIS APPLICATION CONTAINS CLAIMS DIRECTED TO THE FOLLOWING PATENTABLY DISTINCT SPECIES OF THE CLAIMED INVENTION:

A) A LIBRARY (E.G., SPATIALLY ADDRESSABLE PARALLEL SOLID PHASE OR SOLUTION

phase libraries or synthetic libraries made from deconvolution, `one-bead one-compound` methods and by affinity chromatography selection); see claims 3, 13, 25, and 40

b) a bioactive agent (e.g., naturally-occurring compounds, biomolecules, proteins, peptides, oligopeptides, polysaccharides, nucleotides and polynucleotides); see claims 4, 5, 26, and 27)

c) a small molecule; see claims 6 and 28

d) an activator of NFAT-NFAT ligand signaling (e.g., ionomycin, phorbol 12-myristate 13-acetate)

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is required under 35 U.S.C. 121 to elect a single species, even though this requirement is traversed.

The species mentioned above have different and separately burdensome manual and/or computer structure, name, and bibliographical searches, and have divergent subject matter.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, ***AND A LISTING OF ALL CLAIMS READABLE THEREON***, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or

otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Devon R Byrd whose telephone number is 703-305-0159. The examiner can normally be reached on Mon-Fri 8a-5p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 703-306-2317. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

BENNETT CELSA
PRIMARY EXAMINER

DB
October 28, 2003